REMARKS

Claims 2, 3, 5, 9, 14-18, 20-30, and 32-52 are cancelled. Claims 1, 4, 6, 8, 10-13, 19, and 31 are currently pending in the application. Claims 1, 4, 6, 8, 10, 11, and 13 have been amended to further define the claimed subject matter. References to non-elected inventions have been deleted and the claims now specifically refer to the polynucleotides of SEQ ID NO:1 and polynucleotides that encode the amino acid sequence of SEQ ID NO:2. Amended claim 10 finds support in the specification at page 6, lines 15-21 and 27-28. No new matter is added by this amendment.

I. FORMALITIES

The Examiner objected to informalities in the specification. The specification has been amended, removing the space on page 15 and inserting sequence identifiers on pages 27 and 28. The Examiner also objected to claims 1, 2, 4, 6-8, 10-13, 18, 19, 27, 29, and 36 because these claims encompassed nonelected inventions. These claims have been amended or cancelled to remove reference to the nonelected nucleotide sequences.

II. CLAIM REJECTIONS

A. Rejection under 35 U.S.C. § 101

The Examiner rejected claims 1, 2, 4, 6-8, 10-13, 18, 19, 27, 29, 31, and 36 under 35 U.S.C. § 101 as allegedly lacking a credible, specific, and substantial utility. Applicants traverse. A utility of the claimed invention is described in the specification at page 22, lines 7-9, stating that the full-length receptor proteins of the invention may be used to increase BMP activity. Alternatively, as disclosed on page 6, lines 10-11, the truncated proteins of the invention may be used to inhibit BMP activity.

One function of both the full-length and truncated BMP receptors encoded by the claimed nucleotide sequences is to bind BMPs. This function results in the modulation of BMP activity, which may increase (by overexpression of the full-length receptor) or reduce (by using a truncated receptor construct) the ability of BMPs to stimulate, for example, bone and/or cartilage tissue growth. This is a specific utility because only those DNA molecules that encode a BMP-binding protein will be capable of this sort of modulation. And it is a substantial utility because the modulation of the bone and/or cartilage inductive activity of BMPs is a significant "real world" application. For example, increasing bone and/or cartilage growth can assist in healing broken bones or torn cartilage. Alternatively, reducing bone and/or cartilage growth can reduce the symptoms of growth disorders such as hyperthyroidism.

Having established that the disclosed utility is specific and substantial, the only issue is whether it is credible. Specifically, given the totality of the evidence and the reasoning involved, would one of ordinary skill in the art believe that the invention has the disclosed utility? The Examiner says no for the following reasons: (1) the specification allegedly fails to provide objective evidence of any activity for the encoded protein; (2) the specification allegedly does not disclose any activities, diseases, or conditions known to be associated with the encoded protein; and (3) there is allegedly no objective evidence to indicate that the receptor binds BMP-2 or BMP-4 or evidence as to what the consequences of the binding would be.

Applicants disagree. The evidence and reasoning presented in the specification and known to those of skill in the art point to the opposite conclusion—that the encoded proteins bind to BMPs and modulate BMP activity (either by increasing activity with the

full-length receptors or reducing activity with the truncated receptors). This conclusion is based on facts disclosed in the specification, the Examples of the specification, and journal articles that confirm the purported activities of the BMP receptor proteins encoded by the claimed DNA molecules. The specification states that the receptors encoded by the CFK1-23a and CFK1-43a DNA molecules bind to BMP-2 and BMP-4 (page 11, lines 16-18). The Examples describe methods for determining the ability of any given protein to bind to BMPs and methods for determining the ability of a full-length receptor to increase and a truncated receptor to reduce BMP-specific activities such as ectopic bone and cartilage induction. The Examiner has not provided any rationale for doubting the teachings of the specification.

In support of the disclosure of these activities in the specification, journal articles published soon after the priority date of this application confirm that the BMP receptor proteins of the invention do bind to BMPs and do increase BMP activity. We note that the currently claimed nucleotide sequence, named CFK1-23a (SEQ ID NO:1), encodes the protein now known as BMPR-IA. This protein is also known as ALK3 and BRK1.

Chen et al., "DIFFERENTIAL ROLES FOR BONE MORPHOGENETIC PROTEIN (BMP) RECEPTOR TYPE IB AND IA IN DIFFERENTIATION AND SPECIFICATION OF MESENCHYMAL PRECURSOR CELLS TO OSTEOBLAST AND ADIPOCYTE LINEAGES" *J Cell Biol* 142(1):295-305(1998). This article discusses the ability of BMP-2 and BMP-4 to bind to Type IA receptors and the roles of these receptors in mesoderm development. In particular, the article points out that BMPR-IA induces adipocyte differentiation, and that it can ability to transduce BMP signaling when complexed with type II receptors.

Zou et al., "DISTINCT ROLES OF TYPE I BONE MORPHOGENETIC PROTEIN RECEPTORS IN THE FORATION AND DIFFERENTIATION OF CARTILAGE" ***Genes Dev*** **11:2191-2203(1997).** This article describes the function of BMPR-IA in chondrocyte development, showing that a constitutively active form of the receptor causes a delay in chondrocyte differentiation and, when misexpressed, induced irregular differentiation and ossification.

ten Dijke et al., "IDENTIFICATION OF TYPE I RECEPTORS FOR OSTEOGENIC PROTEIN-1 AND BONE MORPHOGENETIC PROTEIN-4." ***J Biol Chem*** **269(25):16985-16988(1994).** This article describes the identification of ALK-3 as a Type I BMP receptor and its ability to bind to BMP-4 when endogenously expressed in mouse osteoblasts and human foreskin fibroblasts.

These three articles demonstrate that the protein encoded by the claimed nucleotide sequences does have the ability to increase BMP activity as disclosed in the specification and does bind to BMP-2 and BMP-4. The articles support the statements made in the specification regarding the utility of the invention and provide incontrovertible evidence of a credible, substantial, and specific utility of the invention.

The Examiner contends that the claimed invention lacks a well-established utility because the limited homology to TGF-β family receptors allegedly does not endow it with a well-established utility because these proteins bind a variety of different agents. Having established a credible, specific, and substantial utility above, Applicants do not need to also provide a rationale for a well-established utility. However, Applicants point out that those of skill in the art are well aware of the growth-inducing properties of BMPs and the details of the mechanisms of TGF-β -TGF-β receptor interactions. The skilled

artisan would expect that, given the homology between TGF-β receptors and BMP receptors, the BMP receptors would have the same utilities, such as inhibiting or assisting BMP activity, just as TGF- β receptors are capable of inhibiting or increasing TGF activity.

Accordingly, Applicants submit that the claimed invention does, in fact, have a credible, specific, substantial, and well-established utility, and request that the Examiner withdraw the rejection under 35 U.S.C. § 101.

The Examiner also rejected claims 6-8 and 11 under 35 U.S.C. § 101 for encompassing non-statutory material. These claims have been amended to require that the host cells be isolated from their host organism, thereby overcoming this rejection.

B. Rejection under 35 U.S.C. § 112, first paragraph: Enablement

The Examiner rejected claims 1, 2, 4, 6-8, 10-13, 18, 19, 27, 29, 31, and 36 as lacking enablement under 35 U.S.C. § 112, first paragraph. The Examiner contends that, due to the alleged lack of utility, the specification also does not teach one of skill in the art how to use the claimed invention. Applicants disagree.

As stated above, the specification contains a credible, specific, and substantial utility, one that is supported by post-filing date references. Furthermore, the specification has also taught one of ordinary skill in the art how to use the invention. On page 13, line 25 to page 14, line 18 the specification describes how to inhibit the effects of BMPs with a protein encoded by the claimed nucleotides. On page 11, line 26 to page 12, line 5, the specification teaches one of skill in the art how to enhance a cell's response to BMPs with a protein encoded by the claimed nucleotides.

These examples of BMP receptor function are easily understood by one of ordinary skill in the art and require no undue experimentation. As stated in the specification, simply expressing the appropriate encoded protein in a cell with inherently produces the desired effect—inhibition or induction of BMP activity. Accordingly, Applicants request that the Examiner withdraw this rejection of the claims under 35 U.S.C. § 112, first paragraph.

Claims 1, 2, 4, 6-8, 10-13, 18, 19, 27, 29, and 36 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement in the specification because the claims encompass sequences that hybridize to SEQ ID NO:1. These claims have been amended and no longer encompass hybridizing sequences. Accordingly, Applicants request that this rejection be withdrawn.

The Examiner also rejected claims 1, 6, 18, 27, 29, and 36 because, prior to Applicants' amendments, these claims encompassed all nucleic acids encoding BMP receptors. These claims have been amended or cancelled, and the amended claims no longer encompass all BMP receptors. Applicants request that this rejection be withdrawn.

The Examiner rejected claim 10 because it encompasses allelic variants. The Examiner contends that there is no guidance as to the structure of these variants and that their structure cannot be predicted from the identification of a single naturally occurring molecule. The allelic variants language has been removed from this claim, thereby overcoming this rejection.

C. Rejections under 35 U.S.C. § 112, first paragraph: Written Description

The Examiner rejected claim 31 under 35 U.S.C. § 112, first paragraph as allegedly lacking written description support in the specification. Specifically, the Examiner indicates that Applicants must provide evidence of the deposit of CFK-123a under the provisions of the Budapest Treaty. Applicants attach proof of such a deposit, a Declaration under 37 C.F.R. § 1.808(a), indicating that the deposit will be made publicly available. Applicants have also have amended the specification to recite the date of the deposit, the complete name and address of the depository, and the accession number of the deposited material. Accordingly, Applicants request that this rejection be withdrawn.

The Examiner also rejected claims 1, 2, 4, 6-8, 10-13, 18, 19, 27, 29, and 36 under 35 U.S.C. § 112, first paragraph as allegedly lacking written description support in the specification. The Examiner contends that the genus of polynucleotides that hybridize to SEQ ID NO:1 or to polynucleotides that encode SEQ ID NO:2 is not adequately described and that "structural features that could distinguish the compounds in the genus from other BMP receptors are missing from the disclosure." Applicants have amended the claims to remove the hybridization language, thereby overcoming this rejection.

The Examiner then contends that claims 1, 6, 18, 27, 29, and 36 are even broader in scope, encompassing all "BMP receptors," including sequences that vary substantially in length and also in composition, which are allegedly not adequately described by the disclosure of the three disclosed nucleic acids. These claims have

been either amended to specifically recite SEQ ID NO:1, or cancelled, thereby overcoming this rejection.

Finally, as above, the Examiner rejection claim 10, alleging that allelic variants of SEQ ID NO:1 are not described in such a way that one of skill in the art would conclude that Applicants were in possession of the claimed genus. This claim has been amended to remove the reference to allelic variants, thereby overcoming this rejection.

Applicants submit that the provision of proof of deposit of the CFK1-23a plasmid according to the Budapest Treaty and the claim amendments overcome the written description rejections under 35 U.S.C. § 112, first paragraph and request that these rejections be withdrawn.

D. Rejections under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 2 and 4 as allegedly indefinite for failing to define "stringent hybridization conditions." Applicants have amended the claims to remove this language. Accordingly, Applicants respectfully request that this rejection be withdrawn.

III. CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

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Dated: 5/27/05

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Attachments:

- Chen et al., *J Cell Biol* 142(1):295-305(1998);
- Zou et al., *Genes Dev* 11:2191-2203(1997);
- ten Dijke et al., *J Biol Chem* 269(25):16985-16988(1994); and
- Declaration under 37 C.F.R. § 1.808(a) and accompanying proof of deposit.